U.S. Measurement System

NIST National Institute of Standards and Technology

Imaging as a Biomarker: Standards for Change Measurements in Therapy

Breakout Area 6: Data Archival & Access Methods: Image, Related Meta-data and Clinical Outcome Data, Related Data Interoperability Standards, and Innovative Methodologies for Data Interpretation

Day 2: Summary

"The Detailed Measurement Science & Standards Needs – The What by When and by Whom"

Near, Mid-Term Issues Only

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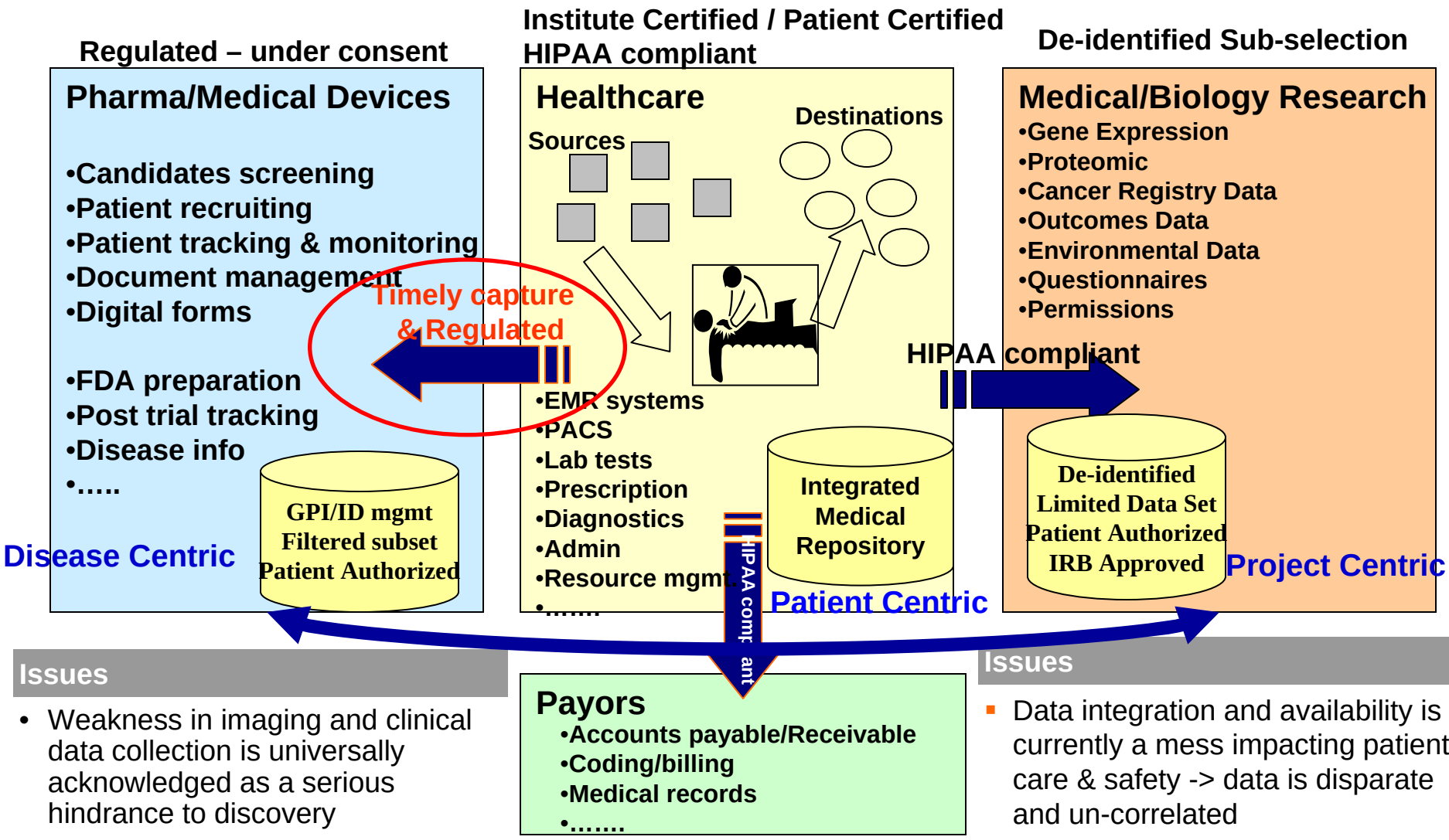
Technology at Issue

1. Research PACS for (more than just) Clinical Trials
2. Legacy PACS for clinical research
3. Data structure and model for data exchange - *21CFR11 compliance*
4. Metadata harmonization, e.g. DICOM - ISO 11179 - CDISC
5. Integration of images and non-image data with quality control = Imaging Biomarker Validation
6. Discovery database

Patient Centric Integrated Repositories – A World of Convergence



Issues

- Weakness in imaging and clinical data collection is universally acknowledged as a serious hindrance to discovery

Issues

- Data integration and availability is currently a mess impacting patient care & safety -> data is disparate and un-correlated

Technology at Issue:
Research PACS
for (more than just) Clinical Trials

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #2 for Near-Term 1-3 Years

1. *Technology at Issue:* Research PACS for (more than just) Clinical Trials
2. *Submitter(s):* Participants of Breakout Area 6
3. *Technological Innovation at Stake: Need research PACS, but most have clinical PACS*
   Reinvent PACS to support clinical research
4. *Economic Significance of Innovation*:
   - Enables and facilitates clinical trial use of images; examples are fMRI scans

   Academic centers may be very interested in Research PACS systems.

   PACS is VERY EXPENSIVE. Complex and difficult to develop.

   Some research scans may NEVER be entered into a clinical PACS!
5. *Technical Barrier to the Innovation*:
   - PACS systems are closed; vendors are not motivated to provide flexible integration of clinical trials data

   No protocols are defined; doesn't support FDA reading paradigm; user identity mgmt is weak; Clinical PACS cannot evolve into a complete clinical research image repository

   Melding of EMR and PACS is underway, but they will remain separate. Deidentification processes are weak. Networking and bandwidth are needed.

   Need support for multitemporal, multimodality longitudinal studies (registration).
6. *Stage of Innovation Where Barrier Appears*:

   Some systems (Impac / Teramedica) exist for radiotherapy that have some clinical research functions.

   What do clinical PACS vendors need to do so the contents can be used in clinical research? Now, the vendor is a barrier. Systems are closed, and don't act effectively as a component of overall system.

Breakout Area 6: Data archival and access methods : Metadata, interoperability standards, interpretation

Measurement Need #2 for Near-Term 1-3 Years (cont'd)

7. *Measurement-Problem Part of Technical Barrier*:

   Research PACS system is not specified. Standards for Research PACS are not defined. Few options for acquisition of such products. Enable data mining of PACS contents. Need to adapt existing standards to Research needs.

8. *Potential Solutions to Measurement Problem:*

   Design and develop research PACS vs.

   Interface a more comprehensive information system with PACS as an embedded component.

9. *Potential Providers of Solutions:*

   PACS vendors; OAI and ADNI must have their own "Research PACS"; ATC may be considered as a "Research PACS" ; caBIG imaging workspace

10. *What is the role for Government, if Any?:*

    Testbeds, specifications, requirements analysis, standards.

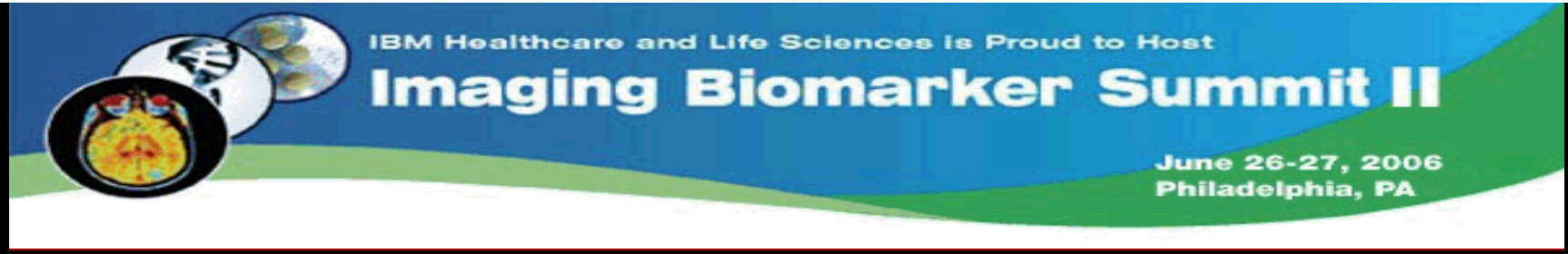
    Policy issues related to access to the data (IRB, privacy)

    IT infrastructure; sponsor host and provide software tools

    Use NCBI Entrez as a model (persistent archive); data + tools sharing stds.

11. *If There is a Government Role, Why Industry Says It Can't/Won't Pay for That Part of Solution:*

    Industry doesn't buy PACS systems, clinical enterprise/ researchers does.



Imaging Data Management Requirements in a Multi-Center Medical Research Environment

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Technology at Issue: Legacy PACS for clinical research

Breakout Area 6: Data archival and access methods : Metadata, interoperability standards, interpretation

Measurement Need #3 for Near-Term 1-3 Years

1. *Technology at Issue:* Legacy PACS for clinical research
2. *Submitter(s):* Participants of Breakout Area 6
3. *Technological Innovation at Stake: Legacy PACS = huge installed base, not suitable for research (has some, but not all necessary data; workflow is not optimal for clinical research)*
4. *Economic Significance of Innovation*:
   - Allows innovative use of images; clinical trials
   - Economics unfavorable; benefits difficult to quantify;

   Post-marketing drug studies require this data.
5. *Technical Barrier to the Innovation*:

   *add-on or add-in; requires PACS redesign (?API); custom GUI needed -- Just a few incremental features are needed!

   DICOM interchange – media; external communications is poor;

   Needs to support deidentification; closed system (security / mission critical)
6. *Stage of Innovation Where Barrier Appears*:

   Hospital IT management is not motivated to help with this.

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #3 for Near-Term 1-3 Years (cont'd)

7. *Measurement-Problem Part of Technical Barrier*:
   - Firewalls are impediment; Need to ensure security and privacy, but allow access to clinical images for research
   - Define incremental changes to PACS needed to satisfy clinical research needs and provide certification process
8. *Potential Solutions to Measurement Problem:*

   Engage PACS vendors and demonstrate the utility of these functions. Secure communication of exported clinical images with a defined interface to closed PACS system. One-way system.
9. *Potential Providers of Solutions:*
   - PACS vendors; IHE; Healthcare IT vendors
10. *What is the role for Government, if Any?:*

    OHRP, part of HHS. Repeal HIPAA (after shooting consultants); Central IRB approval; Define security standards that are universally applicable; Remove liability constraints. Define best practices and supply templates, examples, test data sets. Testbeds. Attend to international harmonization.
11. *If There is a Government Role, Why Industry Says It Can't/Won't Pay for That Part of Solution:*
    - PACS is paid by hospital, which has limited stake in ability to export data. Avoids export due to concerns regarding liability and risk mgmt.

Technology at Issue: Data structure and model for data exchange

21 CFR 11 Compliance

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #1 for Near-Term 1-3 Years

1. *Technology at Issue:* Data structure and model for data exchange - *21CFR11*
2. *Submitter(s):* Participants of Breakout Area 6
3. *Technological Innovation at Stake:*

   21CFR11 compliant image database with audit trail (e.g., RT objects)

   Data management / Data archival system
4. *Economic Significance of Innovation*:
   - FDA will accept; can meet regulatory requirements
   - Costly to implement; use cases are limited
   - Allows company to test new algorithms; compliant repository for testing and certification would significantly reduce cost and time-to-market for CAD and image analysis tools

   Spur innovation by ensuring interoperability among vendors, developers, CROs
5. *Technical Barrier to the Innovation*:
   - DICOM doesn't have audit trail; unwelcome burden for PACS system; content management
   - *Database design that includes audit trail;*
   - *FDA anticipates that images will be reviewed separately due to their size, but the image metadata must be integrated with other forms of data*
6. *Stage of Innovation Where Barrier Appears*:

   For example, software tool developer needs this database when they are testing an innovation intended for submission to FDA

   "Images are a source document" in a regulated clinical trial. (controversial)

   There are degrees of compliance to 21CFR11 databases.

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #1 for Near-Term 1-3 Years (cont'd)

7. *Measurement-Problem Part of Technical Barrier*:

   Testbeds; Defined standards (with FDA oversight) and guidance for images in clinical trials for drug response assessment

8. *Potential Solutions to Measurement Problem:*

   Examples of successful submissions; Statistically robust and validated imaging database solutions that can meet FDA requirements

9. *Potential Providers of Solutions:*

   Healthcare IT vendors; academia and professional societies

10. *What is the role for Government, if Any?:*

    Need Standards and Guidance that users can follow to assemble and submit image collections.

11. *If There is a Government Role, Why Industry Says It Can't/Won't Pay for That Part of Solution:*

    Government is responsible for regulatory decisions; there must be transparency and predictability with standards and quality measures of databases and contents that can meet FDA's decision making requirements

Technology at Issue:
Metadata harmonization

DICOM - ISO 11179 -
CDISC

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #4 for Near-Term 1-3 Years

1. *Technology at Issue:* Metadata harmonization,
   e.g. DICOM - ISO 11179 - CDISC
2. *Submitter(s):* Participants of Breakout Area 6
3. *Technological Innovation at Stake:*
   DICOM and ISO 11179 metadata; CDISC integration of images
4. *Economic Significance of Innovation*:
   Use generic tools to handle image + other biomedical data
   DICOM is effective at interface between modality and PACS; but this value doesn't appear inside PACS.
   CDISC has communications with FDA and is sponsored by Pharma.
5. *Technical Barrier to the Innovation*:
   – caBIG is ISO 11179 compliant, but cancer is pathology driven
   Mapping DICOM to ISO 11179 is verbose, complex, tedious
6. *Stage of Innovation Where Barrier Appears*:
   Integration of data from disparate systems, especially for drug trials.

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #4 for Near-Term 1-3 Years (cont'd)

7. *Measurement-Problem Part of Technical Barrier*:

   Disparate metadata standards, not all of which can use generic software tools and modeling infrastructure

8. *Potential Solutions to Measurement Problem:*

   Harmonization and development of mappings between commonly used established and supported metadata.

9. *Potential Providers of Solutions:*

   CDISC – NIST (experts in ISO 11179 and ISO 15398 multimedia / image standards) - DICOM

10. *What is the role for Government, if Any?:*

    Facilitate harmonization process

11. *If There is a Government Role, Why Industry Says It Can't/Won't Pay for That Part of Solution:*

    Metadata expertise at NIST with generic tools and ISO standards is nonexistent in most healthcare organizations

Technology at Issue: Integration of images and non-image data with quality control

Imaging Biomarker Validation

Breakout Area 6: Data archival and access methods : Metadata, interoperability standards, interpretation

Measurement Need #6 for Near-Term 1-3 Years

1. *Technology at Issue:* Integration of images and non-image data with quality control = Imaging Biomarker Validation
2. *Submitter(s):* Participants of Breakout Area 6
3. *Technological Innovation at Stake: PET, MRI, neuropsych, genetic data over time on same individuals; Establish imaging as a surrogate marker for clinical outcomes. Define image quality.*
4. *Economic Significance of Innovation*:
   - Validation of imaging biomarkers
5. *Technical Barrier to the Innovation*:
   - Need to integrate multitemporal datasets on individuals linked to outcomes
   - Lack of expertise in intrinsics of imaging physics, requires "Imaging Physics Center" with ability to measure quality, qualify sites.
6. *Stage of Innovation Where Barrier Appears*:

Breakout Area 6: Data archival and access methods : Metadata, interoperability standards, interpretation

Measurement Need #6 for Near-Term 1-3 Years (cont'd)

7. *Measurement-Problem Part of Technical Barrier*:
   Standards for exchange of quality control information and centrally monitoring imaging instrument / system performance
8. *Potential Solutions to Measurement Problem:*
   Design and test phantoms with measurement software that provides quantitative centrally reviewed quality results that can be used to assess day-to-day variations from site to site and scanner to scanner
9. *Potential Providers of Solutions:*
   Imaging system vendors; PACS / IT systems vendors
10. *What is the role for Government, if Any?:*
    Define quality standards
11. *If There is a Government Role, Why Industry Says It Can't/Won't Pay for That Part of Solution:*

Technology at Issue:
Discovery database

Breakout Area 6: Data archival and access methods : Metadata, interoperability standards, interpretation

Measurement Need #7 for Near-Term 1-3 Years

1. *Technology at Issue:* Discovery database
2. *Submitter(s):* Participants of Breakout Area 6
3. *Technological Innovation at Stake:*
   Data mining of human clinical trial image collections; enterprise archive
4. *Economic Significance of Innovation*:
   * Better ability for drug development
   Facilitate management decision making regarding "GO-NOGO" after preliminary testing of new agents.
   ** Use prior experience to design new protocols*
   ** Hypothesis generation; CAD tool development and testing (preliminary)*
   Develop innovative methdologies for data mining of these collections;
   Accelerate development and testing of new data analysis methods.
5. *Technical Barrier to the Innovation*:
   Incompatible data in local, private databases; proprietary code in tools
   Sheer bulk of image data is impediment. Lack of integration, need for interfaces.
   Need to develop tools to satisfy the goals.
6. *Stage of Innovation Where Barrier Appears*:
   Reuse of previously collected clinical data; marketing information; early- mid- and late-phase trials; post-market surveillance

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #7 for Near-Term 1-3 Years (cont'd)

7. *Measurement-Problem Part of Technical Barrier*:

   Legacy databases need interfaces and mapping; missing data; data quality standards.

8. *Potential Solutions to Measurement Problem:*

   Data migration from legacy database(s) to a data warehouse or federated data archive with data cleaning and mining tools.

   Combine heterogeneous databases .

9. *Potential Providers of Solutions:*

   NCIA. Healthcare IT vendors (contracted to provide hosts and tools).

10. *What is the role for Government, if Any?:*

    Long term archiving of clinical trial datasets after closure. Define access rights, policies.

11. *If There is a Government Role, Why Industry Says It Can't/Won't Pay for That Part of Solution:*

    Need vanguard projects to demonstrate and test the relevant technologies (ATC has started to do this).

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #5 for Near-Term 1-3 Years

1. *Technology at Issue:*
2. *Submitter(s):* Participants of Breakout Area 6
3. *Technological Innovation at Stake:*

   Capture image-guided treatment plans

4. *Economic Significance of Innovation*:
   - reuse plans; quality control across centers (e.g., rf ablation)
5. *Technical Barrier to the Innovation*:
   - target and day-to-day changes in morphology not defined; borrow on experience of ATC
6. *Stage of Innovation Where Barrier Appears*:

Breakout Area 6: Data archival and access methods : Metadata, interoperability standards, interpretation

Measurement Need #5 for Near-Term 1-3 Years (cont'd)

7. *Measurement-Problem Part of Technical Barrier*:

8. *Potential Solutions to Measurement Problem:*

9. *Potential Providers of Solutions:*

10. *What is the role for Government, if Any?:*

11. *If There is a Government Role, Why Industry Says It Can't/Won't Pay for That Part of Solution:*

Breakout Area 6: Data archival and access methods : Metadata, interoperability standards, interpretation

Measurement Need #1 for Mid-Term 3-5 Years

1. *Technology at Issue:*
2. *Submitter(s):* Participants of Breakout Area 6
3. *Technological Innovation at Stake: Know effects of oncology treatment over time and link to outcomes; flexible ability to add modalities and ancillary data*

4. *Economic Significance of Innovation*:
   - Able to sort out treatment effects from other sources of variation

5. *Technical Barrier to the Innovation*:
   - Difficult to integrate new datasets, rapidly evolving imaging modalities

6. *Stage of Innovation Where Barrier Appears*:

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #1 for Mid-Term 3-5 Years (cont'd)

7. *Measurement-Problem Part of Technical Barrier*:

8. *Potential Solutions to Measurement Problem:*

9. *Potential Providers of Solutions:*

10. *What is the role for Government, if Any?:*

11. *If There is a Government Role, Why Industry Says It Can't/Won't Pay for That Part of Solution:*

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #2 for Mid-Term 3-5 Years

1. *Technology at Issue:*
2. *Submitter(s):* Participants of Breakout Area 6
3. *Technological Innovation at Stake:*

   Linking disparate data in various systems; Query mechanism for multiple databases

4. *Economic Significance of Innovation*:
   - allows interoperation of distributed systems, legacy and newer databases

5. *Technical Barrier to the Innovation*:

6. *Stage of Innovation Where Barrier Appears*:

Breakout Area 6: Data archival and access methods : Metadata, interoperability standards, interpretation

Measurement Need #2 for Mid-Term 3-5 Years (cont'd)

7. *Measurement-Problem Part of Technical Barrier*:

8. *Potential Solutions to Measurement Problem:*

9. *Potential Providers of Solutions:*

10. *What is the role for Government, if Any?:*

11. *If There is a Government Role, Why Industry Says It Can't/Won't Pay for That Part of Solution:*

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #3 for Mid-Term 3-5 Years

1. *Technology at Issue:*
2. *Submitter(s):* Participants of Breakout Area 6
3. *Technological Innovation at Stake:*
   - *Integrate images and receptor ligand maps*

4. *Economic Significance of Innovation*:
5. Targeted drug therapies

5. *Technical Barrier to the Innovation*:

6. *Stage of Innovation Where Barrier Appears*:

Breakout Area 6: Data archival and access methods: Metadata, interoperability standards, interpretation

Measurement Need #3 for Mid-Term 3-5 Years (cont'd)

7. *Measurement-Problem Part of Technical Barrier*:

8. *Potential Solutions to Measurement Problem:*

9. *Potential Providers of Solutions:*

10. *What is the role for Government, if Any?:*

11. *If There is a Government Role, Why Industry Says It Can't/Won't Pay for That Part of Solution:*